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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,791	05/12/2005	Peter G Klimko	2444 US F	8680

7590 01/10/2008

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
01/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,791	KLIMKO ET AL.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received in the office on 9/28/2007. Claim 1 is pending.

Response to Remarks

Applicants' arguments regarding the rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Fridovich et al. (US 2002/0042407) in view of Kato et al. (U.S. 5,665, 769) have been fully considered and found not persuasive. Applicants' arguments regarding the rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Fridovich et al. (WO 99/23097) in view of Kato et al. (U.S. 5,665, 769) have been fully considered and found not persuasive. Applicants' arguments regarding the rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Piganelli et al. (U.S. 2003/0032634) in view of Kato et al. (U.S. 5,665, 769) have been fully considered and found not persuasive. The rejections are maintained and are given below for Applicants' convenience. The action is made Final.

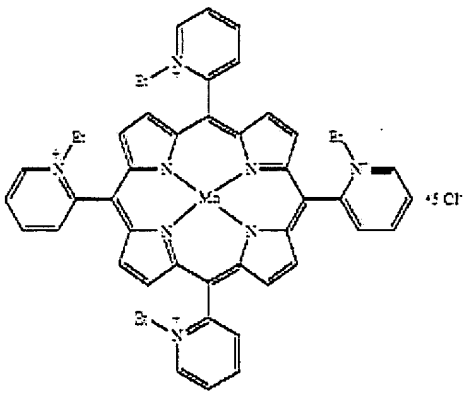
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fridovich et al. (US 2002/0042407) in view of Kato et al. (U.S. 5,665, 769).

Fridovich et al. teach a compound of formula (I) given below (para 0020). The reference further teaches that the mimetics compounds such as formula I are useful in the treatment of diabetes mellitus I or II (para 0020, 0035). The reference further teaches the mimetics compounds can also be used for the treatment of glaucoma, and macular degeneration in the eye (para 0031).



(Formula I)

The reference does not teach the compound in a method of treating diabetic retinopathy.

Kato teaches that among the retinal diseases resulting from systemic diseases, diabetic retinopathy is recognized as one of the diabetic microangiopathies, which are severe complications of diabetes (col. 1, lines 18-20). The reference also teaches macular degeneration, retinal edema and diabetic retinopathy as retinal disorders.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a compound of formula I in a method of treatment of diabetic retinopathy because of the teachings of Fridovich and Kato et al. Fridovich teach the compound of formula I to be useful in the treatment of diabetes and macular

degeneration. Kato et al. teach that macular degeneration, retinal edema and diabetic retinopathy are retinal disorders and diabetic retinopathy as one of the diabetic microangiopathy, a severe complication of diabetes. Hence one of ordinary skill in the art would have been motivated to use the compound of formula I in the treatment of diabetic retinopathy as the compound has been taught to be useful in the treatment of diabetes and another retinal disorder such as macular degeneration and one can expect similar therapeutic benefits or superior results in using the compound in the treatment of diabetic retinopathy.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fridovich et al. (WO 99/23097) in view of Kato et al. (U.S. 5,665, 769).

Fridovich et al. teach the compound of formula I (as above) (page 63, claim 16, formula I). The reference further teaches the compound to be useful in the treatment of edema, and type I and type II diabetes (page 16, lines 1-5).

The reference does not teach the compound in a method of treating diabetic retinopathy.

Kato et al.'s teachings discussed as above.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a compound of formula I in a method of treatment of diabetic retinopathy because of the teachings of Fridovich and Kato et al. Fridovich teach the compound of formula I to be useful in the treatment of diabetes and edema. Kato et al. teach that macular degeneration, retinal edema and diabetic retinopathy are retinal disorders and diabetic retinopathy as one of the diabetic microangiopathy, a severe

complication of diabetes. Hence one of ordinary skill in the art would have been motivated to use the compound of formula I in the treatment of diabetic retinopathy as the compound has been taught to be useful in the treatment of diabetes and another retinal disorder such as retinal edema (a type of edema) and one can expect similar therapeutic benefits or superior results in using the compound in the treatment of diabetic retinopathy.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Piganelli et al. (U.S. 2003/0032634) in view of Kato et al. (U.S. 5,665, 769).

Piganelli et al. teach the compound of formula I (figure 9B) shown above. The reference further teaches the compound to be useful in the prevention, delay the onset of and/or limit the severity of diabetes (p 3, para 0027). The reference also teaches that low molecular weight antioxidants can be used to treat or prevent diabetes-specific microvascular disease of, for example, the retina, renal glomerulus and peripheral nerve (e.g., resulting in oedema, ischaemia and hypoxia-induced neovascularization in the retina (para 0027).

The reference does not teach the compound in a method of treating diabetic retinopathy (DR).

Kato et al.'s teachings discussed as above.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a compound of formula I in a method of treatment of diabetic retinopathy because of the teachings of Piganelli et al. and Kato et al. Piganelli et al. teach the compound of formula I to be useful in the prevention, delay the onset of

and/or limit the severity of diabetes and in the treatment or prevention of diabetes-specific microvascular disease of, for example, the retina. Kato et al. teach diabetic retinopathy as one of the diabetic microangiopathy, a severe complication of diabetes. Hence one of ordinary skill in the art would have been motivated to use the compound of formula I in the treatment of diabetic retinopathy as the compound has been taught to be useful in the treatment or prevention of diabetes-specific microvascular disease of, for example, the retina, and one can expect similar therapeutic benefits or superior results in using the compound in the treatment of diabetic retinopathy.

Response to Arguments

Claim 1 is not obvious over Fridovich (US 2002/0042407) in view of Kato et al. (U.S. 5,665, 769).

Applicants' argue that teaching the use of a compound to treat a particular disease does not make it obvious to use that same compound to treat a particular complication of that disease. Applicants' argue that it would not be obvious to one to use a compound that can treat macular degeneration to treat diabetic retinopathy as they have different characteristics. In response, Fridovich et al. teach a compound of formula (I) and further teaches the mimetics compounds can also be used for the treatment of glaucoma, and macular degeneration in the eye. Fridovich does not teach the compound in a method of treatment of diabetic retinopathy. However Kato teach macular degeneration, retinal edema and diabetic retinopathy as retinal disorders. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention to use the same mimetics compound that Fridovich teaches that can be used

for the treatment of macular degeneration to treat another retinal disorder such as diabetic retinopathy. Kato teaches all of three disorders including macular degeneration and diabetic retinopathy as retinal disorders thus teaching an equivalence and hence it would have been obvious to one of ordinary skill in the art to use a mimetics compound that can be used for the treatment of one retinal disorder for the treatment of another retinal disorder.

Claim 1 is not obvious over Fridovich et al. (WO 99/23097) in view of Kato et al. (U.S. 5,665, 769).

Applicants' argue that teaching the use of a compound to treat a particular disease does not make it obvious to use that same compound to treat a particular complication of that disease. In response, Fridovich et al. teach a compound of formula (I) and further teach the compound to be useful in the treatment of edema. Fridovich does not explicitly teach edema as "retinal edema". Edema is "increase in interstitial fluid in any organ" and retinal edema is "fluid accumulation within the retina". Hence retinal edema is a type of edema which is not excluded from Fridovich's teachings. Kato teach macular degeneration, retinal edema and diabetic retinopathy as retinal disorders. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention to use the same mimetics compound that Fridovich teaches that can be used for the treatment of edema, including retinal edema to treat another retinal disorder such as diabetic retinopathy.

Applicants' argue that Fridovich does not specifically teach or suggest retinal edema can be treated with the compound of formula I. Fridovich does not explicitly

teach edema as “retinal edema”. As stated above, edema is "increase in interstitial fluid in any organ" and retinal edema is "fluid accumulation within the retina". Hence retinal edema is a type of edema which is not excluded from Fridovich's teachings.

Claim 1 is not obvious over Piganelli et al. (U.S. 2003/0032634) in view of Kato et al. (U.S. 5,665, 769).

Applicants' argue that diabetic retinopathy is not only associated with retinal microvascular dysfunction but also with dysfunction of the retinal ganglion cell layer (RGC) and abnormalities in RGC function are frequently observed in diabetes patients before any noticeable vascular related DR symptoms have provided Exhibit A for reference. In response, Antonetti teach that microvascular changes are integral to retinopathy and the retina is a vascularized neural tissue and it is essential to treat both the vascular and neural elements of the retina to preserve vision. Hence it would have been obvious to one of ordinary skill in the art to consider the vascular elements of the retina. Piganelli et al. teach the compound of formula I and further teach the compound can be useful for the treatment of microvascular disease of, for example, the retina, renal glomerulus and peripheral nerve (e.g., resulting in oedema, ischaemia and hypoxia-induced neovascularization in the retina. Oedema or edema as stated above, is "increase in interstitial fluid in any organ" and retinal edema is "fluid accumulation within the retina". Kato teach macular degeneration, edema and diabetic retinopathy as retinal disorders and further teach DR as one of the diabetic microangiopathy, a severe complication of diabetes. Hence one of ordinary skill in the art would have been motivated to use the compound of formula I in the treatment of diabetic retinopathy as

Piganelli et al. teach the compound to be useful in the treatment or prevention of diabetes-specific microvascular disease of, for example, the retina, and odema (another retinal disorder) with expectation of success and achieving similar or superior therapeutic benefits.

Conclusion

No claims are allowed.

The rejections from the previous office action are maintained. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER